

IN THE CLAIMS:

1. (original) A pharmaceutical composition comprising a combination of an inverse agonist of the GABA_A α 5 receptor subtype; a nicotine receptor partial agonist (NRPA), estrogen, selective estrogen modulators, or vitamin E; and a pharmaceutically acceptable carrier.

2. (original) The pharmaceutical composition of claim 1, wherein the inverse agonist has a functional efficacy at the α 5 receptor subtype of less than 20%, and a functional efficacy at the α ₁, α ₂ and α ₃ receptor subtypes of between -20 and +20%.

3. (previously amended) A pharmaceutical composition comprising a combination of an inverse agonist of a GABA α 1 and/or α 5 receptor subtype; a nicotine receptor partial agonist (NRPA), estrogen, selective estrogen modulators, or vitamin E; and a pharmaceutically acceptable carrier; wherein the GABA_A inverse agonist has a functional efficacy at the α 1 and/or α 5 receptor subtypes of less than -5% and the efficacy measured at the α 2 and α 3 receptor subtypes is greater than 5%.

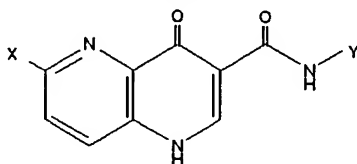
4. (previously amended) The pharmaceutical composition of claim 3, wherein the GABA_A inverse agonist has functional potency (EC₅₀ values) at the α 1 and/or α 5 receptor subtypes of 200 nM.

5. (previously amended) The pharmaceutical composition of claim 3, wherein the GABA_A inverse agonist has a functional efficacy at the α 5 receptor subtype of less than -5%, and the efficacy measured at the α 1, α 2 and α 3 receptor subtypes is greater than 5%.

6. (previously amended) The pharmaceutical composition of claim 5 wherein the GABA_A inverse agonist has a functional potency (EC₅₀ values) at the α 5 receptor subtype of 200 nM.

7. (previously amended) The pharmaceutical composition of claim 3 wherein the GABA_A inverse agonist at the α 1 and/or α 5 receptor subtypes has a binding K_i of 100 nM.

8. (previously amended) The pharmaceutical composition of claim 1, wherein the GABA_A inverse agonist is selected from a compound of Formula I :



wherein:

X is hydrogen, halogen, $-OR_1$, NR_2R_3 , C_1-C_6 alkyl optionally substituted with up to three groups selected independently from halogen and hydroxy, or $-NR_2R_3$; or

X is phenyl, naphthyl, 1-(5,6,7,8-tetrahydro)naphthyl or 4-(1,2-dihydro)indenyl, pyridinyl, pyrimidyl, isoquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, benzofuranyl, benzothienyl, each of which is optionally substituted with up to three groups selected from halogen, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_6 alkylthio, hydroxy, amino, mono or di(C_1-C_6) alkylamino, cyano, nitro, trifluoromethyl; or

X represents a carbocyclic group herein termed "the X carbocyclic group" containing from 3 – 7 atoms, up to two of which are optionally hetero atoms selected from oxygen and nitrogen, where the X carbocyclic group is optionally substituted with one or more groups selected from halogen, (C_1-C_6)alkoxy, mono- or di(C_1-C_6)alkylamino, sulfonamide, aza(C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkylthio, (C_1-C_6)alkylthio, phenylthio, or a heterocyclic group; and

Y is lower alkyl having 1 – 8 carbon atoms optionally substituted with up to two groups selected from halogen, (C_1-C_6)alkoxy, mono- or di(C_1-C_6)alkylamino, sulfonamide, aza(C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkylthio, (C_1-C_6)alkylthio, phenylthio, a heterocyclic group, $-OR_4$, $-NR_5R_6$, SR_7 , or aryl; or

Y is a carbocyclic group herein termed "the Y carbocyclic group" having from 3 – 7 atoms, where up to three of which are optionally hetero atoms selected from oxygen and nitrogen and where any member of the Y carbocyclic group is optionally substituted with halogen, $-OR_4$, $-NR_5R_6$, SR_7 , aryl or a heterocyclic group; and

R_1 is hydrogen, lower alkyl having 1 – 6 carbon atoms, or cycloalkyl having 3 – 7 carbon atoms, wherein each lower alkyl may be optionally substituted with $-OR_4$ or $-NR_5R_6$;

R_2 and R_3 are the same or different and represent hydrogen, lower alkyl optionally mono- or disubstituted with alkyl, aryl, halogen, or mono- or di-lower alkyl; aryl or aryl (C_1-C_6)alkyl where each aryl is optionally substituted with up to three groups selected from halogen, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, or mono- or di(C_1-C_6)alkylamino;

cycloalkyl having 3 – 7 carbon atoms optionally mono or disubstituted with halogen, alkoxy, or mono- or di- lower alkyl; or

$-SO_2R_8$;

R_4 is as defined for R_1 ;

R₅ and R₆ carry the same definitions as R₂ and R₃, respectively;

R₇ is hydrogen, lower alkyl having 1 – 6 carbon atoms, or cycloalkyl having 3 – 7 atoms; and

R₈ is lower alkyl having 1 – 6 carbon atoms, cycloalkyl having 3 – 7 carbon atoms, or optionally substituted phenyl;

or an isomer or hydrate thereof, or a pharmaceutically acceptable salt thereof.

9. (original) The pharmaceutical composition of claim 1, wherein the GABA_A inverse agonist is selected from the group consisting of:

N-n-Butyl-6-chloro-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-n-Butyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Ethylthio)ethyl-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-n-Pentyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-Benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Tetrahydrofuranyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-Isoamyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Methoxybenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Ethoxy)propyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-2-(2-Methyl)butyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-5-Pentanol-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-Benzyl-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4/5-Imidazolyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Thienyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Tetrahydropyranyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3,5-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methoxybenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methylbenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Thienyl)methyl-6-(2-methoxyethoxy)-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Thienyl)methyl-6-morpholino-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Thienyl)methyl-6-dimethylamino-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methylaminomethyl)benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Methylaminomethyl)benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide hydrochloride; and

N-[4-(Imidazolylmethyl)benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide.

10. (original) The pharmaceutical composition of claim 1 in which the NRPA is selected from the group consisting of:

9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-flouro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-ethyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-vinyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-bromo-3-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
3-benzyl-9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
3-benzyl-9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-acetyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-iodo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-cyano-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-ethynyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(2-propenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(2-propyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-carbomethoxy-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-carboxyaldehyde-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(2,6-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(2-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(4-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(3-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(3,5-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(2,4-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
9-(2,5-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
6-methyl-5-oxo-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;

5-oxo-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
 6-oxo-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
 4,5-difluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
 4-ethynyl-5-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 5-ethynyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene-4-carbonitrile;
 6-methyl-5-thia-5-dioxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-
 triene;
 10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 4-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 4-methyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 4-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 4-nitro-10-azatrimethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 7-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
 6-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
 6,7-dimethyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-
 tetraene;
 6-methyl-7-phenyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-
 tetraene;
 6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-
 pentaene;
 5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
 14-methyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-
 pentaene;
 5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
 6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-
 tetraene;
 4-chloro-10-azatrimethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
 10-azatrimethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl cyanide;
 1-(10-azatrimethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;
 10-azatrimethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-ol;
 7-methyl-5-oxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2,4(8),6,9-
 tetraene;
 4,5-dichloro-10-azatrimethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;

11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
 1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-ethanone;
 1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-propanone;
 4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
 5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-4-carbonitrile;
 6-methyl-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
 6-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
 6,7-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
 5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
 5,6-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
 5-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
 6-(trifluoromethyl)-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
 5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
 7-methyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
 6-methyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
 6,7-dimethyl-5,8,15-triazatetracyclo[11.3.1.0^{2,11}.0^{4,9}]heptadeca-2(11),3,5,7,9-pentaene;
 7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
 6-methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
 5-methyl-7-oxa-6,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
 6-methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
 7-methyl-5-oxa-6,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
 4,5-difluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
 4-chloro-5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;

5-chloro-4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
 4-(1-ethynyl)-5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
 5-(1-ethynyl)-4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
 5,6-difluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
 6-trifluoromethyl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
 6-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
 11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-6-ol;
 6-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
 11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-ol;
 4-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
 5-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
 5-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene; and
 6-hydroxy-5-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene and
 their pharmaceutically acceptable salts and their optical isomers.

11. (original) The pharmaceutical composition of claim 1, in which the NRPA is selected from the group consisting of:

9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
 9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
 9-flouro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
 9-acetyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
 9-iodo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
 9-cyano-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;
 9-carbomethoxy-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-carboxyaldehyde-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(2,6-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 9-(2-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;
 6-methyl-5-thia-5-dioxa-6,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,8-triene;
 4-fluoro-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;

4-trifluoromethyl-10-aza-tricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
4-nitro-10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-triene;
6-methyl-5,7,13-triazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,5,8-tetraene;
6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5,8,14-triazatetracyclo[10.3.1.0^{2,11}.0^{4,9}]hexadeca-2(11),3,5,7,9-pentaene;
5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0^{2,10}.0^{4,8}]pentadeca-2(10),3,6,8-tetraene;
10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl cyanide;
1-(10-azatricyclo[6.3.1.0^{2,7}]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;
11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-ethanone;
1-[11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-propanone;
4-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;
5-fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-4-carbonitrile;
6-methyl-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6,7-dimethyl-5,7,14-triazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;
6-methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,6,8-tetraene;
5,6-difluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
6-trifluoromethyl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2,4,6-triene;
6-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
6-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene; and
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-ol and
their pharmaceutically acceptable salts and their optical isomers.

12. (original) The pharmaceutical composition of claim 1, wherein the GABA_A inverse agonist is N-Benzyl-6-ethoxy-4-oxo-1,5-naphthyridine-3-carboxamide, or a

prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug.

Claims 13. - 16. (canceled)

17. (previously presented) The pharmaceutical composition of claim 3 wherein the GABA_A inverse agonist has a functional efficacy at the α 1 and/or α 5 receptor subtypes of less than -10%.

18. (previously presented) The pharmaceutical composition of claim 3 wherein the efficacy measured at the α 2 and α 3 receptor subtypes is greater than 10%.

19. (previously presented) The pharmaceutical composition of claim 3, wherein the GABA_A inverse agonist has functional potency (EC50 values) at the α 1 and/or α 5 receptor subtypes of less than 150 nM.

20. (previously presented) The pharmaceutical composition of claim 3, wherein the GABA_A inverse agonist has a functional efficacy at the α 5 receptor subtype of less than -10%, and the efficacy measured at the α 1, α 2 and α 3 receptor subtypes is greater than 10%.

21. (previously presented) The pharmaceutical composition of claim 5 wherein the GABA_A inverse agonist has a functional potency (EC50 values) at the α 5 receptor subtype of less than 150 nM.

22. (previously presented) The pharmaceutical composition of claim 3 wherein the GABA_A inverse agonist at the α 1 and/or α 5 receptor subtypes has a binding K_i of less than 30 nM.